

Another Potential Risk Factor for ALS: Exposure to Traffic-Related Air Pollutants

Nate Seltenrich

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Little is known about what causes amyotrophic lateral sclerosis (ALS), a rare and debilitating neurological condition affecting approximately 450,000 individuals worldwide.^{1,2} Research suggests that the disease, which has a median survival time of just under three years after the onset of symptoms³ results from a complex set of genetic and exogenous factors;⁴ the vast majority of cases occur in people with no family history.⁴ To date, the best-established risk factor is smoking,⁵ but a report in *Environmental Health Perspectives* offers evidence that exposure to traffic-related air pollutants may also be an important risk factor.⁶

The study included 917 Dutch ALS patients and 2,662 controls from the general population. Using home addresses, the researchers estimated exposures of the participants to six measures of air pollution: the nitrogen oxides NO₂ and NO_x; three measures of particulate matter (PM_{2.5}, PM₁₀, and PM_{coarse}, which is the fraction of PM calculated as the concentration of PM₁₀ minus that of PM_{2.5}); and fine particulate matter absorption (PM_{2.5}absorption, a marker for black soot or carbon).

For all six measures, estimated exposures were higher for ALS patients than for controls. Similarly, for the three measures most closely associated with traffic—NO_x, NO₂, and PM_{2.5}absorption—individuals in the most-exposed group were more likely to have been diagnosed with ALS than those in the least-exposed group. All estimated pollutant levels fell below current European limits.⁶

The size of the estimated effects of NO₂ and PM_{2.5}absorption was similar to or higher than what previous studies have shown for smoking, says lead author and physician Meinie Seelen, who performed the research while earning her PhD at Utrecht University. The stronger association with traffic-related particles, which are the smallest of the pollutants measured, makes biological sense, she says.

“It has been demonstrated that ultrafine particles can circumvent the blood–brain barrier,” Seelen says. She explains that the tiny particles are deposited in the lining of the nose, and there is evidence that they may travel from there to the brain via the olfactory nerve.⁷ Previous research has shown that this may, in turn, cause chronic brain inflammation, oxidative stress, and other outcomes that could contribute to ALS.^{8,9,10}

But there may be something else going on as well, says Jane Parkin Kullmann, a University of Sydney postgraduate researcher and toxicologist who studies behavioral and environmental factors in ALS. Traffic-related pollution often contains metals, including lead and mercury, as a result of processes such as the wearing of brakes and tires.¹¹ These metals are known to be toxic to the brain.^{12,13}

“As far as the biological rationale, it is very different for lead or mercury versus ultrafine particles; their mode of action is different,” says Kullmann, who was not involved with the present



Smoking is currently the best-established risk factor for amyotrophic lateral sclerosis (ALS). In a new study, exposures to three traffic-related pollutants had estimated effects on ALS that were similar to or higher than smoking. Image: © georgeclerk/iStockphoto.

study. But ultimately, she notes, exposures to a combination of metals and fine particles—as opposed to just one pollutant or the other—could potentially play a role in ALS.

The new research adds to the results from an epidemiological study published in 2015 that investigated the relationship between air pollution and ALS occurrence.¹⁴ That study also reported an association, though in a far smaller population of 51 patients. Evelyn Talbott, senior author of the 2015 paper and a professor of epidemiology at the University of Pittsburgh, says the new study is a landmark in the field.

“The methodology was impressive, and they certainly performed a number of different sensitivity analyses,” she says. “It is a strong paper. Now that this has been done once, I am sure other people are going to look at the same thing.” In addition to replicating the study among different populations, future work could use animal models to investigate potential mechanisms, says Talbott, who also was not involved with the present study.

Future research could also seek to shed light on the still-shrouded etiology of ALS by investigating not only the potential role of pollution but also critical windows of exposure, says Roel Vermeulen, a professor at Utrecht University and senior author of the new paper. “Besides replication, the more nuanced questions also still have to be answered,” he says. “Is air pollution earlier in life or later in life more important? Is it a trigger, or does it accelerate? These are [aspects] that we do not know.”

Some previous epidemiological studies have already linked exposure to air pollution with incidence of Parkinson and Alzheimer diseases, the two most common neurodegenerative diseases.^{15,16,17,18} “It is possible,” suggests lead author Seelen, “that air pollution represents the first in a chain of events, although not necessarily the most important one.”

Nate Seltenrich covers science and the environment from Petaluma, California. His work has appeared in *High Country News*, *Sierra*, *Yale Environment 360*, *Earth Island Journal*, and other regional and national publications.

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